

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for the treatment of a disease mediated by p38 other than cancer, comprising administering a compound of formula I



wherein B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X_n ,

wherein n is 0-3 and each X is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{NO}_2$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted $\text{C}_2\text{-C}_{10}$ alkenyl, substituted $\text{C}_1\text{-C}_{10}$ alkoxy, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl and $-\text{Y-Ar}$;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NO}_2$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ and halogen up to per-halosubstitution;

wherein R^5 and $\text{R}^{5'}$ are independently selected from H, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, up to per-halosubstituted $\text{C}_1\text{-C}_{10}$ alkyl, up to per-halosubstituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, up to per-halosubstituted $\text{C}_2\text{-C}_{10}$ alkenyl, up to per-halosubstituted $\text{C}_6\text{-C}_{14}$ aryl and up to per-halosubstituted $\text{C}_3\text{-C}_{13}$ heteroaryl,

wherein Y is $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^5)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^5)-$, $-\text{O}(\text{CH}_2)_m-$, $-\text{CHX}^a$, $-\text{NR}^5\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})-$,

$-\text{C}(\text{O})\text{NR}^5-$, $-\text{CX}^{\text{a}}_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^5)(\text{CH}_2)_m-$,

$m = 1-3$, and X^{a} is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1} ,

wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})-\text{NR}^5$, $-\text{NO}_2$, $=\text{O}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{SO}_2\text{R}^5$, $-\text{SO}_2\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^5$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_7\text{-C}_{24}$ alkaryl and substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^{5'}$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $=\text{O}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NO}_2$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^5$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_4\text{-C}_{24}$ alkheteroaryl and $\text{C}_7\text{-C}_{24}$ alkaryl

A is a heteroaryl moiety selected from the group consisting of

SR⁴, -NR⁴R^{4'}, -C(O)R⁴, -CO₂R⁴, -C(O)NR⁴R^{4'}, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ heteroaryl; and

wherein R⁴ and R^{4'} are independently selected from the group consisting of H, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl; C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ heteroaryl,

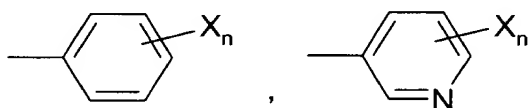
R^a is C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl and up to per-halosubstituted C₃-C₁₀ cycloalkyl; and

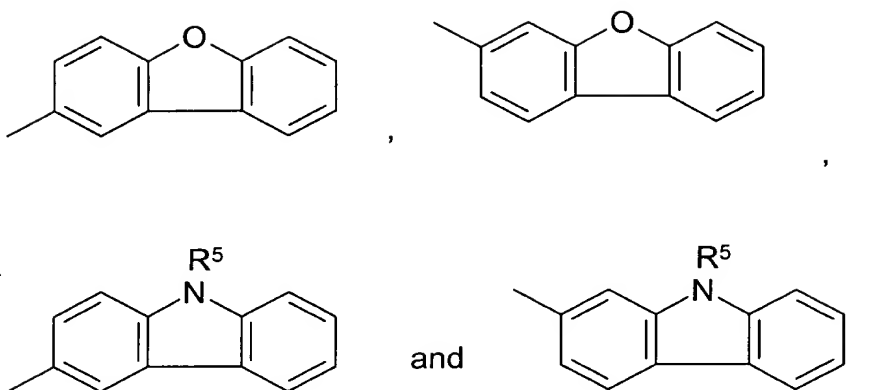
R^b is hydrogen or halogen,

R₁₀₀ is selected from the group consisting of halogen, tert-butyl, C₃-C₁₀ cycloalkyl, C₁-C₁₃ heteroaryl, C₆₋₁₄ aryl, C₇₋₂₄ alkaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₃ heteroaryl, up to per-halosubstituted C₆₋₁₄ aryl, and up to per-halosubstituted C₇₋₂₄ alkaryl;

R^c is hydrogen, halogen, C₁-C₁₀ alkyl, up to per-halosubstituted C₁-C₁₀ alkyl or combines with R¹ and the ring carbon atoms to which R¹ and R^c are bound to form a 5- or 6-membered cycloalkyl, aryl or hetaryl ring with 0-2 members selected from O, N and S.

2. (Original) A method as in claim 1, wherein B is up to a tricyclic aromatic ring structure selected from the group consisting of





which is substituted or unsubstituted by halogen, up to per-halosubstitution, and

wherein $n = 0-3$ and each X is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{NO}_2$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, C_{2-10} -alkenyl, C_{1-10} -alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, and substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted C_{2-10} -alkenyl, substituted C_{1-10} -alkoxy, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl and $-\text{Y-Ar}$;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, NO_2 , $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ and halogen up to per-halosubstitution;

wherein R^5 and $\text{R}^{5'}$ are independently selected from H , $\text{C}_1\text{-C}_{10}$ alkyl, C_{2-10} -alkenyl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, up to per-halosubstituted $\text{C}_1\text{-C}_{10}$ alkyl, up to per-halosubstituted C_{2-10} -alkenyl, up to per-halosubstituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, up to per-halosubstituted $\text{C}_6\text{-C}_{14}$ aryl and up to per-halosubstituted $\text{C}_3\text{-C}_{13}$ heteroaryl,

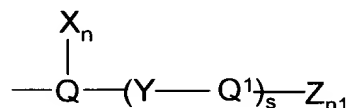
wherein Y is $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^5)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-\text{NR}^5\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{NR}^5-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^5)-$, $-\text{O}(\text{CH}_2)_m-$, $-\text{CHX}^a$, $-\text{CX}^a_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^5)(\text{CH}_2)_m-$,

$m = 1-3$, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halo and

optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $=\text{O}$, $-\text{SO}_2\text{R}^5$, $-\text{SO}_2\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{NO}_2$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_7\text{-C}_{24}$ alkaryl and substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl; wherein if Z is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $=\text{O}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NO}_2$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, C-C_{10} heteroaryl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_4\text{-C}_{24}$ alkheteroaryl and $\text{C}_7\text{-C}_{24}$ alkaryl.

3. (Previously Presented) A method of claim 1, wherein B is



wherein Y is selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{CH}_2-$, $-\text{SCH}_2-$, $-\text{CH}_2\text{S}-$, $-\text{CH}(\text{OH})-$, $-\text{C}(\text{O})-$, $-\text{CX}^a_2$, $-\text{CX}^a\text{H}-$, $-\text{CH}_2\text{O}-$ and $-\text{OCH}_2-$, where X^a is halogen,

Q is a six member aromatic structure containing 0–2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

Q^1 is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0–4 members of the group consisting of N, O and S, unsubstituted or unsubstituted by halogen up to per-halosubstitution, and

X, Z, n and $n1$ are as defined in claim 1 and s is 0 or 1.

4. (Original) A method as in claim 3, wherein

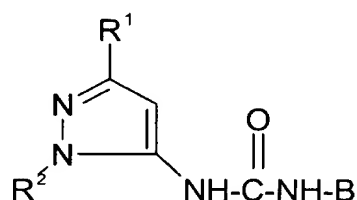
Q is phenyl or pyridinyl, substituted or unsubstituted by halogen, up to per-halosubstitution,

Q^1 is selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, substituted or unsubstituted by halogen, up to

per-halo substitution, or -Y-Q¹ is phthalimidinyl substituted or unsubstituted by halogen up to per-halo substitution, and

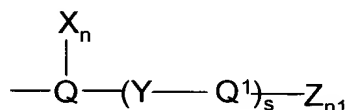
Z and X are independently selected from the group consisting of -R⁶, -OR⁶ and -NHR⁷, wherein R⁶ is hydrogen, C₁-C₁₀-alkyl or C₃-C₁₀-cycloalkyl and R⁷ is selected from the group consisting of hydrogen, C₃-C₁₀-alkyl, C₃-C₆-cycloalkyl and C₆-C₁₀-aryl, wherein R⁶ and R⁷ can be substituted by halogen or up to per-halosubstitution.

5. (Original) A method as in claim 1, comprising administering a compound of the formula



wherein R¹ and R² and B are as defined in claim 1.

6. (Previously Presented) A method as in claim 5, wherein B is 2,3-dichlorophenyl or of the formula



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O-, -S-, -CH₂- or -SCH₂, X is CF₃, and Z is -OH, -Cl or NHC(O)-C_pH_{2p+1}, where p = 2-4, s = 0 or 1, n = 0 and n₁ = 0 or 1.

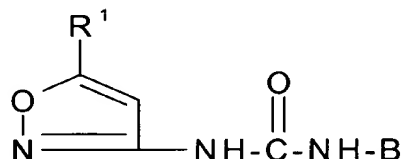
7. (Original) A method as in claim 1 comprising administering a compound selected from the group consisting of:

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(2,3-dichlorophenyl)urea;
N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;
N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;
N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;
N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;
N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichlorophenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-hydroxy-phenyl)thiophenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-ethylaminocarbonyl-phenyl)oxyphenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-isobutylaminocarbonyl-phenyl)thiophenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)thio-3-(trifluoromethyl)phenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;
N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-((4-pyridinyl)methylthio)-phenyl)urea;
N-(1-(2,2,2-Trifluoroethyl)-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichloro-phenyl)urea;
N-(1-(2-Hydroxyethyl)-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichlorophenyl)urea;
N-(1-Ethoxycarbonylmethyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichloro-phenyl)urea;
N-(1-(2-Cyanoethyl)-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichlorophenyl)urea;
N-(1-(3-Hydroxyphenyl)methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichloro-phenyl)urea;
N-(1-Cyclohexyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)methyl-phenyl)urea;
N-(1-methyl-3-phenyl-5-pyrazolyl)-*N'*-(3-(4-(2-methylcarbamoyl)-pyridyl)thiophenyl) urea;
N-(1-methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridyl)thiophenyl) urea;
N-(1-methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-(4-pyridyl)thiophenyl) urea;
N-(1-methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-trifluoromethyl-4-(4-pyridylthio)phenyl) urea;

N-(3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-(4-pyridyl)oxyphenyl) urea;
N-(3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;
 and pharmaceutically acceptable salts thereof.

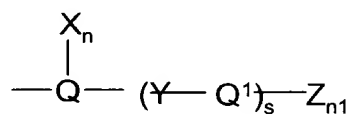
8. (Original) A method as in claim 5, wherein R¹ is t-butyl.

9. (Original) A method as in claim 1 comprising administering a compound of the formula



wherein R¹ and B are as defined in claim 1.

10. (Original) A method as in claim 9, wherein B is



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O-, -S- or -CH₂, X is CF₃, Z is OH, CH₃, - O-C_pH_{2p+1}, wherein n = 2-6 or -C(O)-NH-CH₃, s = 1, n = 0 or 1 and n1 = 0 or 1.

11. (Original) A method as in claim 1 comprising administering a compound selected from the group consisting of:

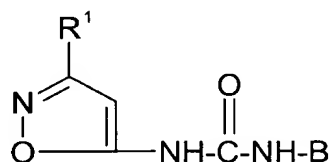
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-hydroxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-isopropoxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-isobutoxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-pentyloxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-methylaminocarbonylphenyl)-oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(3-(4-pyridinyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(4-pyridinyl)thio-3-(trifluoromethyl)-phenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(3-(3-methyl-4-pyridinyl)thiophenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(3-(3-methyl-4-pyridinyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(3-methyl-4-pyridinyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-isoxazolyl)-*N'*-(4-(3-methyl-4-pyridinyl)thiophenyl)urea;
N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(4-(4-(2-methylcarbamoyl)pyridyl)-oxyphenyl) urea;
N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(3-(4-(2-methylcarbamoyl)-pyridyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(4-(4-(2-carbamoyl)pyridyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(3-(4-(2-carbamoyl)pyridyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(3-((4-pyridyl)fluoromethyl)phenyl) urea;
N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(3-((4-pyridyl)oxomethyl)phenyl) urea;

and pharmaceutically acceptable salts thereof.

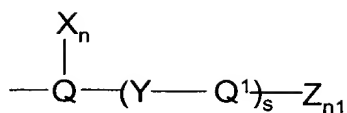
12. (Original) A method as in claim 9, wherein R¹ is t-Butyl.

13. (Original) A method as in claim 1 comprising administering a compound of the formula



wherein R¹ and B are as defined in claim 1.

14. (Previously Presented) A method as in claim 13, wherein B is 2,3-dichlorophenyl or of the formula



wherein Q is phenyl, Q¹ is phenyl, pyridinyl or benzothiazolyl, Y is -O-, -S-, -CH₂- or -NH-, Z is Cl, -CH₃ or -OCH₃, s = 0 or 1, n = 0 and n₁ = 0 or 1.

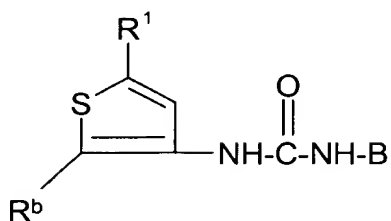
15. (Original) A method as in claim 13, wherein R¹ is t-butyl.

16. Original) A method as in claim 1 comprising administering a compound selected from the group consisting of :

N-(3-Isopropyl -5-isoxazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;
N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(2,3-dichlorophenyl)urea;
N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-methoxyphenyl)aminophenyl)urea;
N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-methoxyphenyl)oxyphenyl)urea;
N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;
N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;
N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;
N-(3-(1,1-Dimethylpropyl)-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)methyl-phenyl)urea;
N-(3-(1,1-Dimethylpropyl)-5-isoxazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;
N-(3-(1,1-Dimethylpropyl)-5-isoxazolyl)-*N'*-(4-(2-benzothiazolyl)-oxyphenyl)urea;
N-(3-(1-Methyl-1-ethylpropyl)-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)oxy-phenyl)urea;
N-(3-(1-Methyl-1-ethylpropyl)-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)methyl-phenyl)urea;
N-(3-cyclobutyl-5-isoxazolyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;
N-(3-*tert*-butyl-5-isoxazolyl)-*N'*-(4-(4-pyridyl)thiophenyl) urea;
N-(3-(1-methyl-1-ethylprop-1-yl)-5-isoxazolyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;
N-(3-*tert*-butyl-5-isoxazolyl)-*N'*-(4-(4-pyridyl)methylphenyl) urea;
N-(3-*tert*-butyl-5-isoxazolyl)-*N'*-(4-(4-methoxyphenyl)aminophenyl) urea;

and pharmaceutically acceptable salts thereof.

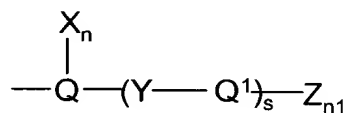
17. (Currently Amended) A method as in claim 1 comprising administering a compound



of the formula

wherein R^b is hydrogen and R¹, R^b and B are as defined in claim 1.

18. (Original) A method as in claim 17, wherein B is of the formula



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O- or -S- or -CH₂-, Z is OH, CH₃, Cl, -OC₂H₅ or -OC₃H₇, s = 0 or 1, n = 0 and n₁ = 0 or 1.

19. (Original) A method as in claim 17, wherein R¹ is t-butyl.

20. (canceled)

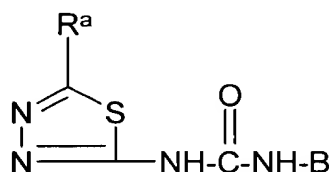
21. (Original) A method as in claim 1 comprising administering a compound selected from the group consisting of:

N-(2-Bromo-5-*tert*-butyl-3-thienyl)-*N'*-(4-methylphenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(2,3-dichlorophenyl)urea;

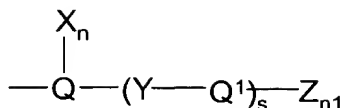
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-hydroxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-ethoxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-isopropoxyphenyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(3-pyridinyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;
N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;
N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(4-(4-pyridyl)oxyphenyl) urea;
N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(3-(4-pyridyl)thiophenyl) urea;
N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(3-(4-methoxyphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(3-(4-methylphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-pyridyl)thiophenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-pyridyl)methylphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(2,3-dichlorophenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-hydroxyphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-methoxyphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-ethoxyphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-isopropoxyphenyl)oxyphenyl) urea;
 and pharmaceutically acceptable salts thereof.

22. (Original) A method as in claim 1 comprising administering a compound of the formula



wherein R^a and B are as defined in claim 1.

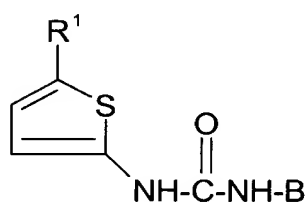
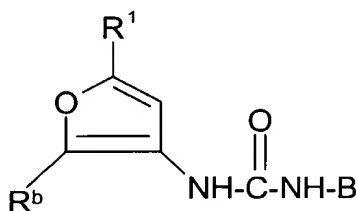
23. (Original) A method as in claim 22, wherein B is of the formula



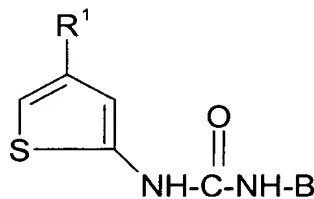
wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O-, -S- or CH₂-, Cl, -OC₂H₅ or -OC₃H₇, s = 0 or 1, n = 0 and n₁ is 0 or 1.

24. (Original) A method as in claim 22, wherein R^a is CF₃- or t-butyl.

25. (Currently Amended) A method as in claim 1 comprising administering a compound of one of the formulae

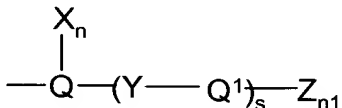


or



wherein R^b is hydrogen and R¹, R^b and B are as defined in claim 1.

26. (Original) A method as in claim 25, wherein B is of the formula



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O-, -S- or -CH₂-, Z is OH, CH₃, Cl, -OC₂H₅ or -OC₃H₇, s = 0 or 1, n = 0 and n₁ is 0 or 1.

27. (Original) A method as in claim 25, wherein R¹ is t-butyl.

28. (Previously Presented) A method as in claim 1, wherein the compound for formula I displays p38 IC₅₀'s of less than 10 μ m as determined by an in-vitro p38 kinase inhibition assay.

29. (Previously Presented) A method according to claim 1, wherein the disease is mediated by a cytokine and/or protease (proteolytic enzyme) regulated by p38.

30. (Original) A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit p38.

31. (Previously Presented) A method according to claim 29, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

32. (Original) A method according to claim 1, wherein the disease is mediated by TNF α , MMP-1, MMP-3, IL-1, IL-6 or IL-8.

33. (Original) A method according to claim 1, wherein the disease is an inflammatory or immunomodulatory disease.

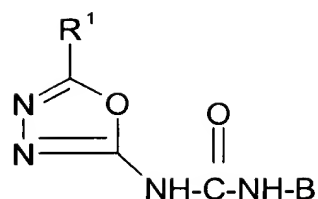
34. (Original) A method according to claim 1, wherein the disease is rheumatoid arthritis, osteoporosis, osteoarthritis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions.

35. Canceled

36. Canceled

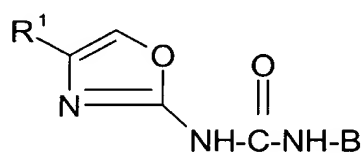
37. (Original) A method as in claim 1, comprising administering a compound of the

formula



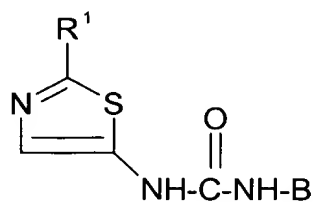
wherein R¹ and B are as defined in claim 1.

38. (Original) A method as in claim 1 comprising administering a compound of the formula



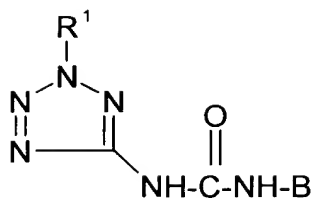
wherein R¹ and B are as defined in claim 1.

39. (Original) A method as in claim 1, comprising administering a compound of the formula



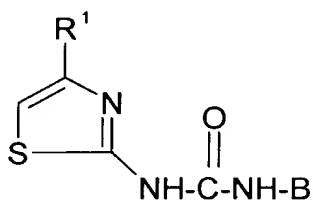
wherein R¹, R² and B are as defined in claim 1.

40. (Original) A method as in claim 1, comprising administering a compound of the formula



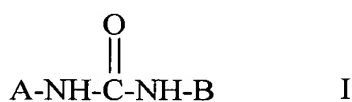
wherein R¹ and B are as defined in claim 1.

41. (Original) A method as in claim 1, comprising administering a compound of the formula



wherein R¹ and B are as defined in claim 1.

42. (Currently Amended) A method for the treatment of a disease mediated by p38 other than cancer comprising administering a compound of formula I



wherein B is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X_n, wherein n is 0-3 and each X is independently selected from the group consisting of -CN, -CO₂R⁵, -C(O)NR⁵R^{5'}, -C(O)R⁵, -NO₂, -OR⁵, -SR⁵, -NR⁵R^{5'}, -NR⁵C(O)OR^{5'}, -NR⁵C(O)R^{5'}, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl

up to per halo-substituted C₁-C₁₀ alkyl, up to per halo-substituted C₂-C₁₀ alkenyl, up to per halo-substituted C₁-C₁₀ alkoxy, up to per halo-substituted C₃-C₁₀ cycloalkyl, and -Y-Ar;

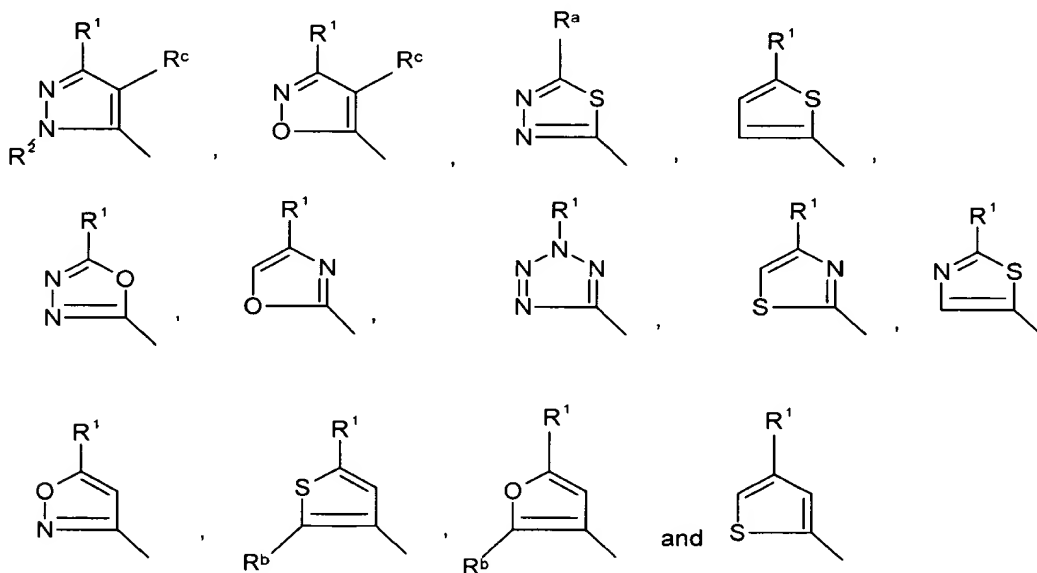
wherein R⁵ and R^{5'} are independently selected from H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₂-C₁₀ alkenyl_[5] and up to per-halosubstituted C₃-C₁₀ cycloalkyl,

wherein Y is - O-, -S-, -N(R⁵)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -NR⁵C(O)NR⁵ NR^{5'}-, -NR⁵C(O)-, -C(O)NR⁵-, -(CH₂)_mS-, -(CH₂)_mN(R⁵)-, -O(CH₂)_m-, -CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁵)(CH₂)_m-,

m = 1-3, and X^a is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, =O, -CO₂R⁵, -C(O)NR⁵R^{5'}, -C(O)-NR⁵, -NO₂, -OR⁵, -SR⁵, -NR⁵R^{5'}, -NR⁵C(O)OR^{5'}, -C(O)R⁵, -NR⁵C(O)R^{5'}, -SO₂R⁵, SO₂NR⁵R^{5'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, up to per halo-substituted C₁-C₁₀ alkyl, and up to per halo-substituted C₃-C₁₀ cycloalkyl, and

A is a heteroaryl moiety selected from the group consisting of



wherein

R^1 is selected from the group consisting of halogen, C_3 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_1 - C_{13} heteroaryl, C_6 - C_{14} aryl, C_7 - C_{24} alkaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{13} heteroaryl, up to per-halosubstituted C_6 - C_{14} aryl, and up to per-halosubstituted C_7 - C_{24} alkaryl;

R^2 is selected from the group consisting of H, $-C(O)R^4$, $-CO_2R^4$, $-C(O)NR^3R^{3'}$, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, substituted C_1 - C_{10} alkyl, substituted C_3 - C_{10} cycloalkyl, substituted C_7 - C_{24} alkaryl and substituted C_4 - C_{23} alkheteroaryl,

where R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-CN$, $-CO_2R^4$, $-C(O)NR^3R^{3'}$, $-NO_2$, $-OR^4$, $-SR^4$, and halogen up to per-halosubstitution,

wherein R^3 and $R^{3'}$ are independently selected from the group consisting of H, $-OR^4$, $-SR^4$, $-NR^4R^{4'}$, $-C(O)R^4$, $-CO_2R^4$, $-C(O)NR^4R^{4'}$, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, , phenyl, pyridinyl, naphthyl, isoquinolinyl or quinolinyl

up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, and up to per-halosubstituted, phenyl, pyridinyl, naphthyl, isoquinolinyl or quinolinyl and

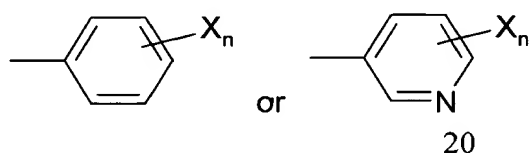
wherein R^4 and $R^{4'}$ are independently selected from the group consisting of H, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, , phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, and up to per-halosubstituted, phenyl, pyridinyl, naphthyl, isoquinolinyl or quinolinyl,

R^a is C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{10} alkyl and up to per-halosubstituted C_3 - C_{10} cycloalkyl; and

R^b is hydrogen or halogen,

R^c is hydrogen, halogen, C_1 - C_{10} alkyl, up to per-halosubstituted C_1 - C_{10} alkyl or combines with R^1 and the ring carbon atoms to which R^1 and R^c are bound to form a 5- or 6-membered cycloalkyl, aryl or hetaryl ring with 0-2 members selected from O, N and S.

43. (Previously Presented) A method as in claim 42, wherein B is



which is substituted or unsubstituted by halogen, up to per-halosubstitution, and wherein

$$n = 1-3 \text{ and}$$

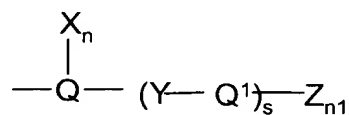
each X is independently selected from the group consisting of C₁₋₄ alkyl, up to per-halosubstituted C₁₋₄ alkyl and -Y-Ar;

wherein Y is -O-, -S-, -N(R⁵)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -NR⁵C(O)NR⁵NR^{5'}-, -NR⁵C(O)-, -C(O)NR⁵-, -(CH₂)_mS-, -(CH₂)_mN(R⁵)-, -O(CH₂)_m-, -CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁵)(CH₂)_m-,

m = 1-3, and X^a is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, =O, -CO₂R⁵, -C(O)NR⁵R^{5'}, -C(O)R⁵, -NO₂, -OR⁵, -SR⁵, -NR⁵R^{5'}, -NR⁵C(O)OR^{5'}, -C(O)R⁵, -NR⁵C(O)R^{5'}, -SO₂R⁵, -SO₂R⁵R^{5'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, up to per halo-substituted C₁-C₁₀ alkyl, and up to per halo-substituted C₃-C₁₀ cycloalkyl, wherein R⁵ and R^{5'} are independently selected from H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₂-C₁₀ alkenyl and up to per-halosubstituted C₃-C₁₀ cycloalkyl.

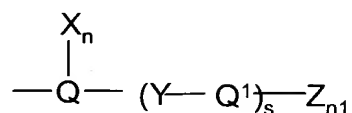
44. (Previously Presented) A method as in claim 5, wherein B is of the formula



wherein Q is phenyl or pyridinyl, optionally substituted by halogen up to per-halosubstitution, Q¹ is pyridinyl, phenyl or benzothiazolyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S-, -CH₂S-, -SCH₂-, -CH₂O-, -OCH₂- or -CH₂-, X is C₁-C₄ alkyl or

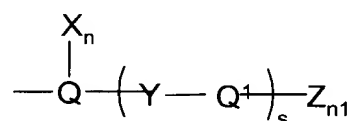
up to per-halosubstituted C₁-C₄ alkyl and Z is as defined in claim 1, n = 0 or 1, s = 1 and n₁ = 0-1.

45. (Previously Presented) A method as in claim 9, wherein B is of the formula



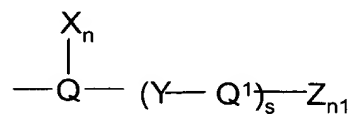
Q is phenyl or pyridinyl, optionally substituted by halogen up to per-halosubstitution, Q¹ is pyridinyl, phenyl or benzothiazolyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S-, -C(O)- or -CH₂-, X is C₁-C₄ alkyl or up to per-halosubstituted C₁-C₄ alkyl and Z is as defined in claim 1 n = 0 or 1, s = 0 or 1 and n₁ = 0 or 1.

46. (Previously Presented) A method as in claim 13, wherein B is of the formula



Q is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Q¹ is phenyl, benzothiazolyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S- or -CH₂-, X is C₁-C₄ alkyl or up to per-halosubstituted C₁-C₄ alkyl, Z is as defined in claim 1, n = 0 or 1, s = 1, and n₁ = 0 or 1.

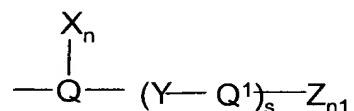
47. (Previously Presented) A method as in claim 17, wherein B is of the formula



wherein Q is phenyl optionally substituted by halogen up to per-halosubstitution, Q¹ is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Y is -O- or -S-, X is C₁-C₄

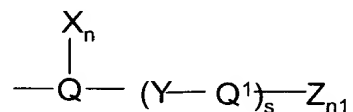
alkyl or up to per-halosubstituted C₁-C₄ alkyl, Z is as defined in claim 1, n = 0 or 1, s = 0 or 1 and n₁ = 0-2.

48. (Previously Presented) A method as in claim 22, wherein B is of the formula



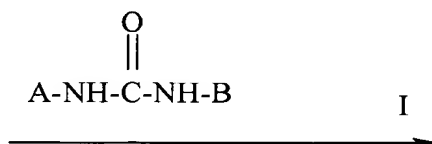
wherein Q is phenyl optionally substituted by halogen up to per-halosubstitution, Q¹ is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, Y is -O- or -S-, X is C₁-C₄ alkyl or up to per-halosubstituted C₁-C₄ alkyl, s = 1, Z is as defined in claim 1, n = 0 or 1 and n₁ = 0 or 1.

49. (Previously Presented) A method as in claim 28, wherein B is of the formula



wherein Q is phenyl optionally substituted by halogen up to per-halosubstitution, Q¹ is phenyl or pyridinyl optionally substituted by halogen up to per-halosubstitution, and Y is -O- or -S-, X is C₁-C₄ alkyl or up to per-halosubstituted C₁-C₄ alkyl, Z is as defined in claim 1, n = 0 or 1 s = 0 or 1 and n₁ = 0-2.

50. (Currently amended) A method ~~as in claim 1,~~ for the treatment of a disease mediated by p38 other than cancer, comprising administering a compound of formula I



wherein B is

a) phenyl, pyridinyl, naphthyl, quinolinyl or isoquinolinyl, substituted by -Y-Ar and optionally substituted by

- halogen up to per-halosubstitution,
- C₁-C₄ alkyl,
- up to per-halosubstituted C₁-C₄ alkyl, or
- a combination thereof,

wherein Y and Ar are as defined in claim 1;

wherein Y is -O-, -S-, -N(R⁵)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-,
-(CH₂)_mS-, -(CH₂)_mN(R⁵)-, -O(CH₂)_m-, -CHX^a, -NR⁵C(O)NR⁵R^{5'}-, -NR⁵C(O)-,
-C(O)NR⁵-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁵)(CH₂)_m-,

m = 1-3, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1},

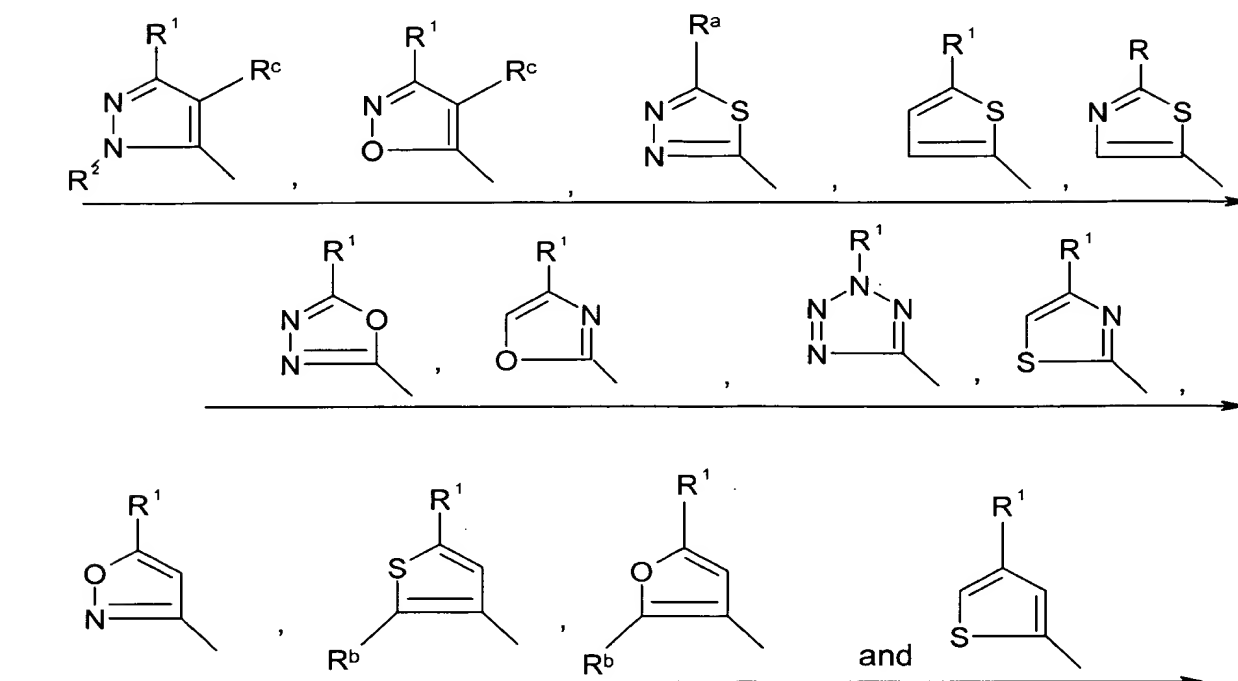
wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁵, -C(O)NR⁵R^{5'}, -C(O)-NR⁵, -NO₂, =O, -OR⁵, -SR⁵, -NR⁵R^{5'}, -C(O)R⁵, -SO₂R⁵, -SO₂NR⁵R^{5'}, -NR⁵C(O)OR^{5'}, -NR⁵C(O)R^{5'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, substituted C₁-C₁₀ alkyl, substituted C₃-C₁₀ cycloalkyl, substituted C₇-C₂₄ alkaryl and substituted C₄-C₂₃ alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of -CN, -CO₂R⁵, -C(O)R^{5'}, -C(O)NR⁵R^{5'}, =O, -OR⁵, -SR⁵, -NO₂, -NR⁵R^{5'}, -NR⁵C(O)R^{5'}, -NR⁵C(O)OR^{5'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C-C₁₀ heteroaryl, C₆-C₁₄ aryl, C₄-C₂₄ alkheteroaryl and C₇-C₂₄ alkaryl

b) thienyl substituted by methyl; or

e) indolyl substituted by phenyl or pyridyl

A is a heteroaryl moiety selected from the group consisting of



wherein

R¹ is selected from the group consisting of halogen, C₃-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₁-C₁₃ heteroaryl, C₆₋₁₄ aryl, C₇₋₂₄ alkaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₃ heteroaryl, up to per-halosubstituted C₆₋₁₄ aryl, and up to per-halosubstituted C₇₋₂₄ alkaryl;

R² is selected from the group consisting of H, -C(O)R⁴, -CO₂R⁴, -C(O)NR³R^{3'}, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₇₋₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, substituted C₁-C₁₀ alkyl, substituted C₃-C₁₀ cycloalkyl, substituted C₇₋₂₄ alkaryl and substituted C₄-C₂₃ alkheteroaryl,

where R² is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁴, -C(O)-NR³R^{3'}, -NO₂, -OR⁴, -SR⁴, and halogen up to per-halosubstitution,

wherein R³ and R^{3'} are independently selected from the group consisting of H, -OR⁴, -SR⁴, -NR⁴R^{4'}, -C(O)R⁴, -CO₂R⁴, -C(O)NR⁴R^{4'}, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl, C₇₋₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and

up to per-halosubstituted C₃-C₁₃ heteroaryl; and

wherein R⁴ and R^{4'} are independently selected from the group consisting of H, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ heteroaryl,

R^a is C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl and up to per-halosubstituted C₃-C₁₀ cycloalkyl; and

R^b is hydrogen or halogen,

R^c is hydrogen, halogen, C₁-C₁₀ alkyl, up to per-halosubstituted C₁-C₁₀ alkyl or combines with R¹ and the ring carbon atoms to which R¹ and R^c are bound to form a 5- or 6-membered cycloalkyl, aryl or hetaryl ring with 0-2 members selected from O, N and S.

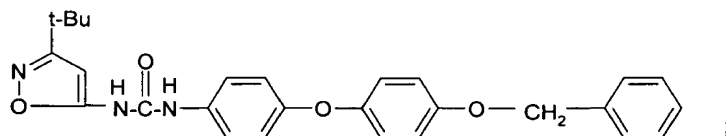
51. (Previously Presented) A method as in claim 1, wherein B is phenyl or pyridinyl substituted by -Y-Ar and optionally substituted by

- halogen ,up to per-halosubstitution,
- C₁-C₄ alkyl,
- up to per-halosubstituted C₁-C₄ alkyl, or
- a combination thereof,

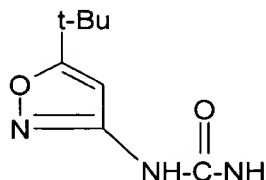
wherein Y and Ar are as defined in claim 1.

52. (Currently amended) A compound of claim 1 of one of the formulae

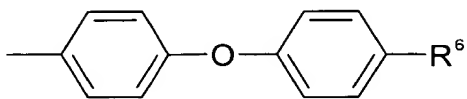
a)



b)

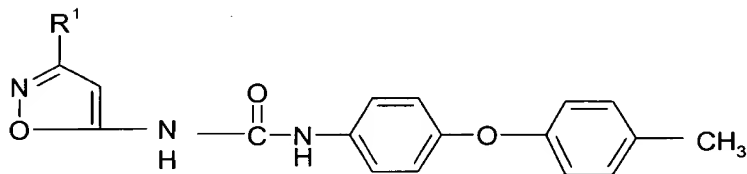


wherein R^6 is $-O-CH_2$ -phenyl, $-NH-C(O)-O$ -t-butyl, $-O$ -n-pentyl, $-O$ -n-butyl,



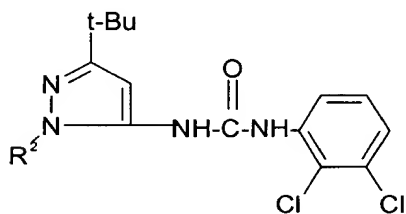
$-C(O)-N(CH_3)_2$, $-O-CH_2CH(CH_3)_2$ or $-O$ -n-propyl;

c)

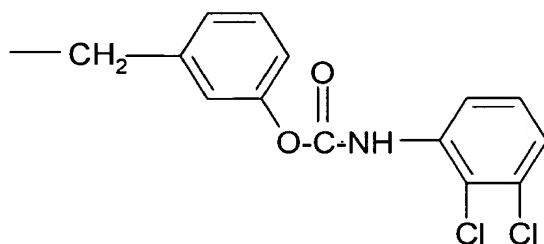


wherein R^1 is $-CH_2$ -t-butyl;

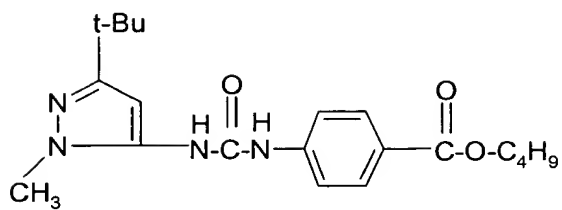
d)



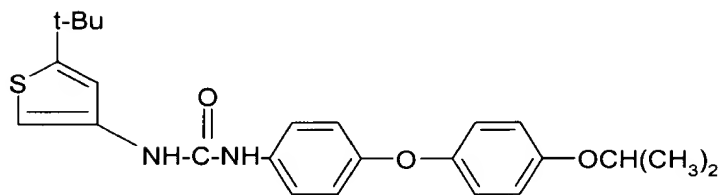
wherein R^2 is $-CH_2CF_3$, $-C_2H_4$ $-OH$, $-CH_2-(3-HOC_6H_4)$, $-CH_2C(O)NHCH_3$, $-CH_2C(O)OC_2H_5$, $-C_2H_4CN$, or



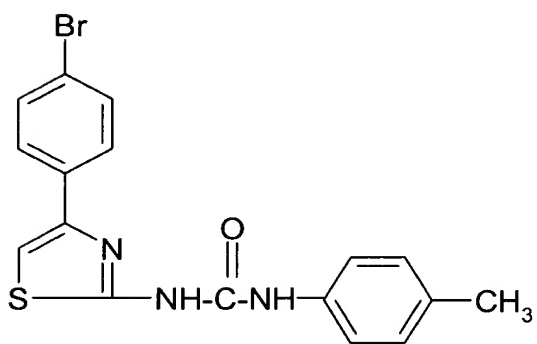
e)



f)

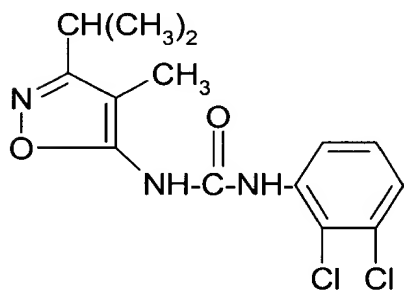


g)



or

h)



and pharmaceutically acceptable salts thereof.

53. (Previously Presented) A pharmaceutical composition comprising a compound according to claim 52 or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

54. (Previously Presented) A method according to claim 1, wherein R^b is hydrogen.

55. (Currently Amended) A method according to claim 1, wherein R^{100} is selected from the group consisting of halogen, C_3 - C_{10} cycloalkyl, C_1 - C_{13} heteroaryl, C_{6-14} aryl, C_{7-24} alkaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{13} heteroaryl, up to per-halosubstituted C_{6-14} aryl, and up to per-halosubstituted C_{7-24} alkaryl.

56. (canceled)

57. (Previously Presented) A method according to claim 42, wherein R^1 is selected from the group consisting of halogen, C_3 - C_{10} cycloalkyl, C_1 - C_{13} heteroaryl, C_{6-14} aryl, C_{7-24} alkaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{13} heteroaryl, up to per-halosubstituted C_{6-14} aryl, and up to per-halosubstituted C_{7-24} alkaryl.